Concentrations of selected antimicrobials in caecum, colon and manure of pigs due to a 3 % cross-contamination of the feed

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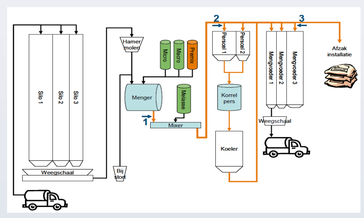
Introduction



3%

Pig feed may contain up to 3% carry-over of the recommended therapeutic concentrations of antimicrobials[1] as a result of contamination between medicated and non-medicated feed. Gut concentrations due to this cross-contamination with chlortetracycline, doxycycline and sulfadiazine-trimethoprim were investigated.

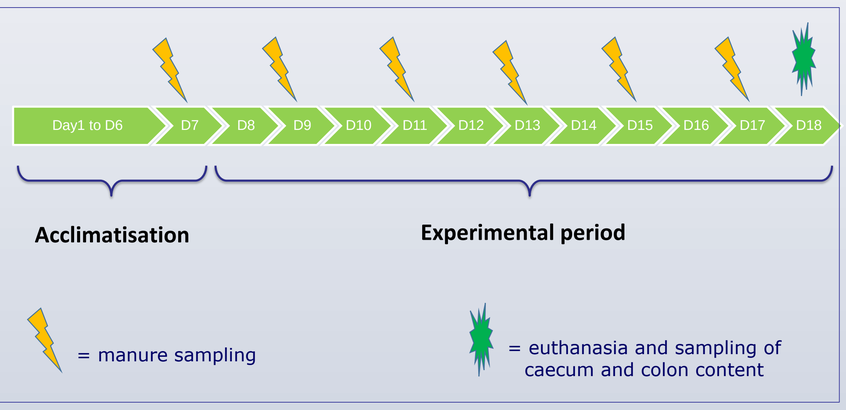
[1]Based on the EU guideline regarding coccidiostats or histomonostats (2009/8/EG). Since 2013, limits of 1% of minimal therapeutic concentrations are applied in Belgium.

Materials and methods

1. Preparation of 3 batches of **experimental feed** with a 3% carry-over level of the recommended therapeutic dose of following antimicrobials: doxycycline, sulfadiazine-trimethoprim and chlortetracycline. For each batch, 10 samples were analysed using in-house developed and validated LC-MS/MS methods.

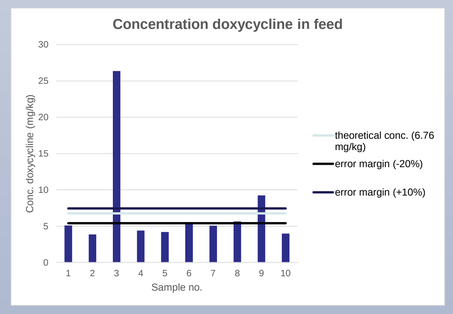
2. Animal experiment

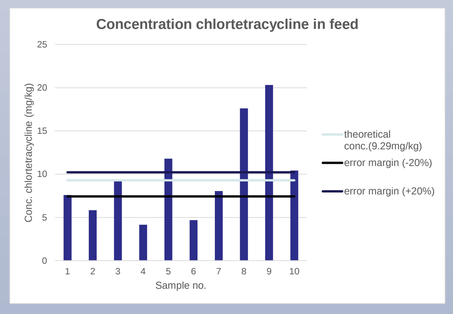
Twenty-four pigs were equally divided into one control group and three experimental groups receiving experimental feed during 10 days. Every two days, individual manure samples were taken and individual colon and caecum content was sampled on day 11. Samples were analysed using in-house developed and validated LC-MS/MS methods.



Results

Homogeneity of the experimental feed



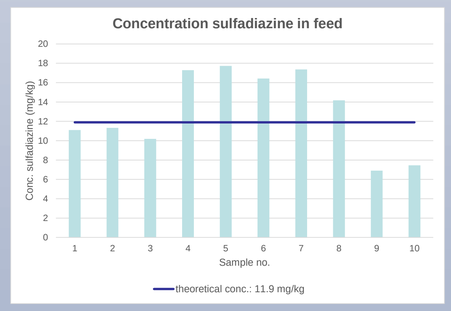


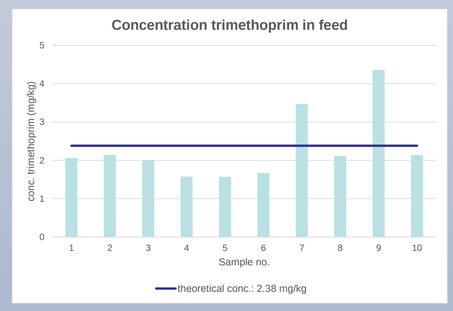
+ chlortetracycline

+ doxycycline

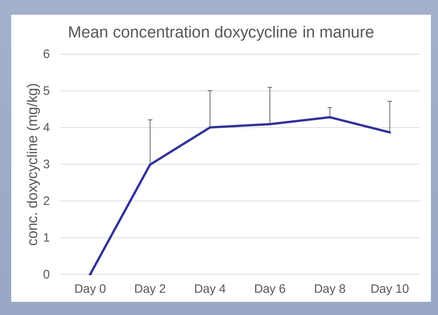
+ sulfadiazine-trimethoprim

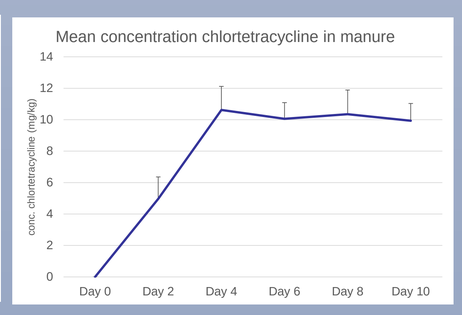
Average antimicrobial concentrations in all 3 batches approached the intended concentrations. However, high variations between different samples were found.





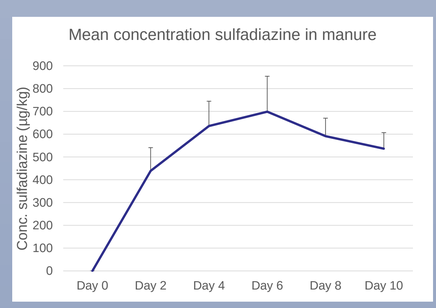
Antimicrobial concentrations in manure





Mean concentrations (+/- SD) of each antimicrobial rose to a steady state on day 4 of:

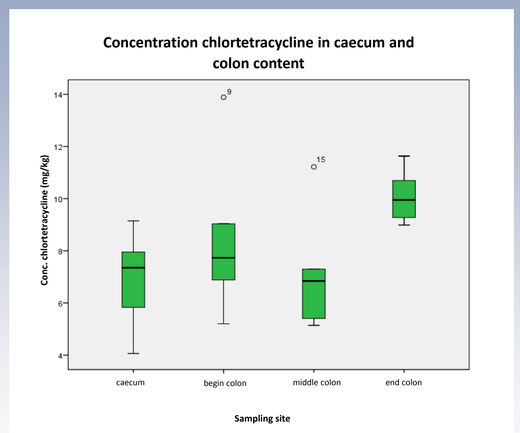
- → 4 mg/kg wet weight (w.w.) for **doxycycline**
- → 10 mg/kg w.w. for **chlortetracycline**
- → 500-700 µg/kg w.w. for **sulfadiazine**
- → **Trimethoprim**: all values were below the limit of detection, no quantification

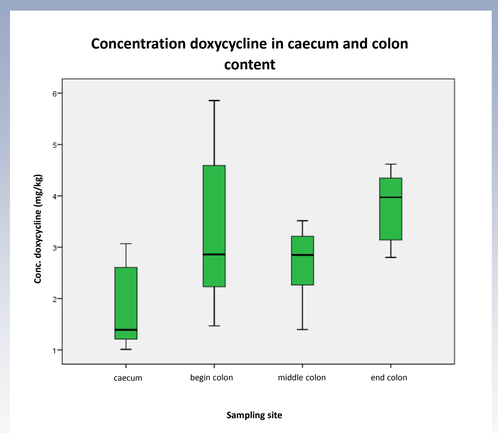


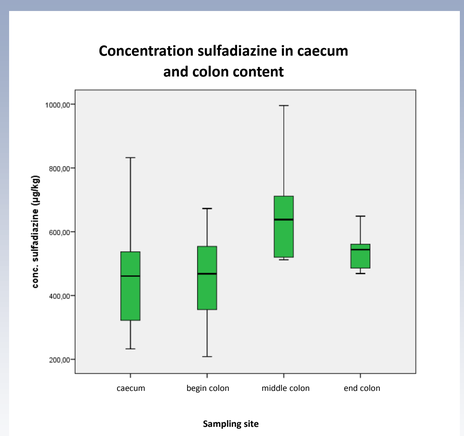
Antimicrobial concentrations in caecum and colon content

- Mean concentration of 6 observations/sampling site
- CI 95%

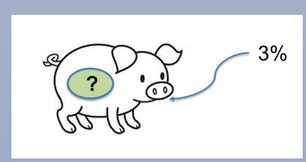
- Mean concentration end colon ~ mean concentration manure for all antimicrobials tested
- **Tetracycline** concentrations are relatively **high** in general and highest concentrations are found in end colon
- **Sulfadiazine** concentrations are relatively **low** in general and highest concentrations are found in middle colon
- **Trimethoprim**: all values were below the limit of detection, no quantification







Transfer ratio's (TR)



TR manure =

$$\frac{Mean\ concentration\ manure\ (*)}{Mean\ concentration\ in\ feed}$$

(*) day 2 – day 10 of experimental period

TR caecum and colon content =

$$\frac{Mean\ concentration\ caecum\ and\ colon\ content}{Mean\ concentration\ in\ feed}$$

Transfer ratio (TR) of antimicrobials compared to their oral bioavailability (BA) in pigs

Antimicrobial	TR Caecum / colon content	TR Manure	BA
Chlortetracycline	82%	92%	6%
Doxycycline	39%	52%	20%
Sulfadiazine	4.1%	4.5%	80-100%
Trimethoprim	ND	ND	60-80%

Conclusions

These data show that the poor oral bioavailabilities of tetracyclines may result in rather high concentrations in caecum, colon and manure, even at 3% cross-contamination of the feed. As expected, the high oral bioavailabilities of sulfadiazine and trimethoprim appear to result in very low gut concentrations. Research on the effects of these concentrations on the gut flora is ongoing.

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